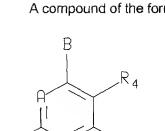
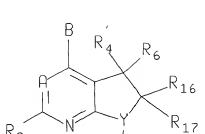
CLAIMS

1. A compound of the formula

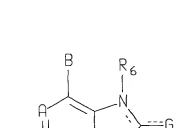


I



II

or



III

or a pharmaceutically acceptable salt thereof, wherein

the dashed lines represent optional double bonds, with the proviso that when the dashed line in C---G represent a double bond, then the dashed line in N(R_8)---C does not represent a double bond; and with the proviso that when the dashed line in N(R_8)---C represents a double bond, R_8 is absent in formula III and the dashed line in C---G does not represent a double bond;

A is -CR_7 or N;

B is -NR_1R_2, -$CR_1R_2R_{11}$, -$C(=CR_2R_{12})R_1$, -$NHCHR_1R_2$, -$OCHR_1R_2$, -$SCHR_1R_2$, -CHR_2OR_1, -CHR_1OR_2, -CHR_2SR_1, -$C(S)R_2$, -$C(O)R_2$, -$CHR_2NR_1R_2$, -CHR_1NHR_2, -$CHR_1N(CH_3)R_2$, or -$NR_{12}NR_1R_2$;

when the dashed line in C---G represents a double bond, then G is hydrogen, oxygen, sulfur, NH, or $N(C_1-C_4$ alkyl);

when the dashed line in C---G does not represent a double bond, then C---G is -C(H)(NH_2), CH_2, -C(H)(methoxy), -C(H)(ethoxy), -C(H)(O(C_3-C_4 alkyl)), -C(H)(halo), -C(H)(trifluoromethoxy), -C(H)(methyl), -C(H)(ethyl), -C(H)(C_3-C_4 alkyl), -C(H)(S(C_1-C_4 alkyl)), -C(C_1-C_4 alkyl)(C_1-C_4 alkyl), cyclopropyl, -C(H)(cyclopropyl), thiomethoxy, -C(H)(NH_2), -C(H)($NHCH_3$), -C(H)($N(CH_3)_2$), or –C(H)(trifluoromethyl);

wherein said cyclopropyl, methoxy, ethoxy, C_3-C_4 alkyl, and C_1-C_4 alkyl groups of C---G may optionally be substituted by one OH, methoxy, or trifluoromethoxy, or may optionally be substituted by from one to six fluoro atoms;

Y is CH or N;

Z is NH, O, S, -N(C_1-C_2 alkyl), -NC(O)CF_3, or -C($R_{13}R_{14}$), wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or -C($R_{13}R_{14}$) is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5, which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR_{12}, and $S(O)_m$, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C_1-C_4 alkyl, -O(C_1-C_4 alkyl), NH_2, $NHCH_3$, $N(CH_3)_2$, CF_3, or OCF_3, with the proviso that said ring does not contain any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and does not comprise more than two oxygen or $S(O)_m$ heterologous members;

R_1 is C(O)H, C(O)(C_1-C_6 alkyl), C(O)(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), C(O)(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), C(O)(C_1-C_6 alkylene)(C_4-C_8 heterocycloalkyl), -C(O)(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_1-C_6 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), or –O-aryl, or –O-(C_1-C_6 alkylene)-aryl; wherein said aryl, C_4-C_8 heterocycloalkyl, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylene, and C_1-C_6 alkylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 alkyl, -C_3-C_8 cycloalkyl, hydroxy, chloro, bromo, iodo, CF_3, -O-(C_1-C_6 alkyl), -O-(C_3-C_5 cycloalkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(R_{24})(R_{25}), -N(R_{24})(R_{25}), -S(C_1-C_4 alkyl), -S(C_3-C_5 cycloalkyl), -N(C_1-C_4alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl), -COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I^-, -SO(C_1-C_4 alkyl) and -SO_2(C_1-C_4 alkyl); and wherein the C_1-C_6 alkyl, C_1-C_6 alkylene, C_5-C_8 cycloalkyl, C_5-C_8 cycloalkylene, and C_5-C_8 heterocycloalkyl moieties of R_1 may optionally independently contain from one to three double or triple bonds; and wherein the C_1-C_4 alkyl

moieties and C_1-C_6 alkyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, -CH_2-aryl, C_3-C_5 cycloalkyl, or –O-(C_1-C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocycloalkyl group of R_1 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

R_2 is hydrogen, C_1-C_{12} alkyl, C_3-C_8 cycloalkyl, C_4-C_8 heterocycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_1-C_6 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, –(C_1-C_6 alkylene)aryl, or -(C_3-C_8 cycloalkylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, -OH, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_6 alkyl), -S(O)(C_1-C_6 alkyl), -S(O)$_2$(C_1-C_6 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I^-, CN, and NO_2; and wherein the C_1-C_{12} alkyl, -(C_1-C_6 alkylene), -(C_5-C_8 cycloalkyl), -(C_5-C_8 cycloalkylene), and -(C_5-C_8 heterocycloalkyl) moieties of R_2 may optionally independently contain from one to three double or triple bonds; and wherein each heterocycloalkyl group of R_2 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

or when R_1 and R_2 are as in –NHCHR_1R_2, -OCHR_1R_2, -SCHR_1R_2, –CHR_1R_2 or -NR_1R_2, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12}; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1-C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3, -O-(C_1-C_4 alkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -S(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl),-COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO$_2$(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), and –SO$_2$(C_1-C_4 alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, NH_2, NH(C_1-C_2 alkyl), N(CH_3)$_2$, -NHCOCF_3, -NHCH_2CF_3, S(O)$_m$(C_1-C_4 alkyl), $CONH_2$, -CONHCH_3, CON(CH_3)$_2$, -CF_3, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 alkyl, C_3-C_5 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR_{24}, C_1-C_6 alkoxy, -O-(C_3-C_5 cycloalkyl), -O-(C_1-C_4 alkylene)(C_3-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), -CH_2SC(S)O(C_1-C_4 alkyl), -CH_2OCF_3, CF_3, amino, nitro, -N$R_{24}R_{25}$, -(C_1-C_4 alkylene)-OR_{24}, -(C_1-C_4 alkylene)Cl, -(C_1-C_4 alkylene)N$R_{24}R_{25}$, -NHCOR_{24}, -NHCON$R_{24}R_{25}$, -C=NOR_{24}, -NHN$R_{24}R_{25}$, -S(O)$_m$$R_{24}$, -C(O)$R_{24}$, -OC(O)$R_{24}$, -C(O)CN, -C(O)N$R_{24}R_{25}$, -C(O)NHN$R_{24}R_{25}$, and –

$COOR_{24}$, wherein the alkyl and alkylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCH_3$, $-NHCOCH_2Cl$, $-NH(C_1-C_2$ alkyl), $-N(C_1-C_2$ alkyl)$(C_1-C_2$ alkyl), $-COO(C_1-C_4$ alkyl), -COOH, $-CO(C_1-C_4$ alkyl), C_1-C_6 alkoxy, C_1-C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1-C_{10} alkyl, $-(C_1-C_4$ alkylene)$(C_3-C_8$ cycloalkyl), $-(C_1-C_4$ alkylene)$(C_4-C_8$ heterocycloalkyl), $-(C_3-C_8$ cycloalkyl), $-(C_4-C_8$ heterocycloalkyl), $-(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), $-(C_3-C_8$ cycloalkylene)$(C_4-C_8$ heterocycloalkyl), C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CO(NOR_{22})R_{23}$, $-CO_2R_{26}$, $-C{=}N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1-C_{10} alkyl, C_3-C_8 cycloalkyl, $(C_1-C_4$ alkylene), $(C_3-C_8$ cycloalkyl), $(C_3-C_8$ cycloalkylene), and $(C_4-C_8$ heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected form C_1-C_4 alkyl, C_3-C_8 cycloalkyl, $(C_1-C_4$ alkylene)$(C_3-C_8$ cycloalkyl), $-(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), C_1-C_4 haloalkyl, hydroxy, C_1-C_6 alkoxy, nitro halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R^5, which ring optionally can contain one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any –S-S-, -O-O-, -S-O-, or –N-S- bonds, and which ring is optionally substituted with C_1-C_4 alkyl, C_3-C_8 cycloalkyl, $-(C_1-C_4$ alkylene)$(C_3-C_8$ cycloalkyl), $-(C_3-C_8$ cyloalkylene)$(C_3-C_8$ cycloalkyl), C_1-C_4 haloalkyl, nitro, halo, cyano $-NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{26})R_{25}$, or $-S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27} can further be selected from $-SO_2NH(C_1-C_4$ alkyl), $-SO_2NH(C_1-C_4$ alkylene)$(C_3-C_8$ cycloalkyl), $-SO_2NH(C_3-C_8$ cycloalkyl), $-SO_2NH(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), $-SO_2N(C_1-C_4$ alkyl)$(C_1-C_2$ alkyl), $-SO_2NH_2$, $-NHSO_2(C_1-C_4$ alkyl), $-NHSO_2(C_3-C_8$ cycloalkyl), $-NHSO_2(C_1-C_4$ alkylene)$(C_3-C_8$ cycloalkyl), and $-NHSO_2(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl); and wherein the alkyl, and alkylene groups of R_5 may independently optionally contain one double or triple bond;

R_6 is hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, $-(C_1-C_6$ alkylene)$(C_3-C_8$ cycloalkyl), or $-(C_3-C_8$ cycloalkylene)$(C_3-C_8$ cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or, wherein the compound is a compound of formula II, R_6 and R_4 can together form an oxo (=O) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous

ring members selected from O, SO_m, N, and NR_{12}, but not containing any –O-O-, -S-O-, -S-S-, or –N-S- bonds, and further optionally substituted with C_1-C_4 alkyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 alkyl substituent may optionally contain one double or triple bond;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C_1-C_2 alkyl), -O(cyclopropyl), -COO(C_1-C_2 alkyl), -COO(C_3-C_8 cycloalkyl), -OCF_3, CF_3, -CH_2OH, or CH_2OCH_3;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl;

R_{16} and R_{17} are each, independently, hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that R_{16} and R_{17} are not both methoxy or ethoxy;

or R_{16} and R_{17} together form an oxo (=O) group;

or R_{16} and R_{17} are connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing from one to three heterologous ring members selected from O, SO_m, N, and NR_{12}, but not containing any –O-O-, -S-O-, -S-S-, or –N-S- bonds, and further optionally substituted with C_1-C_4 alkyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 alkyl substituent may optionally contain one double or triple bond;

R_{22} is independently at each occurrence selected from hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4 alkylene)(C_3-C_8 cycloalkyl);

R_{23} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_2-C_8 alkoxyalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, -(C_1-C_4 alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R_{24} and R_{25} are independently at each occurrence selected from hydrogen, -C_1-C_4 alkyl, C_1-C_4 haloalkyl, especially CF_3, -CHF_2, CF_2CF_3, or CH_2CF_3, -(C_1-C_4 alkylene)OH, -(C_1-C_4 alkylene)-O-(C_1-C_4 alkyl), -(C_1-C_4 alkylene)-O-(C_3-C_5 cycloalkyl), C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -C_4-C_8 heterocycloalkyl, -(C_1-C_4 alkylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl), wherein the -C_4-C_8 heterocycloalkyl groups can each independently optionally be substituted with aryl, CH_2-aryl, or C_1-C_4 alkyl, and can optionally contain one or two double or triple bonds; or, when R_{24} and R_{25} are as $NR_{24}R_{25}$, -C(O)$NR_{24}R_{25}$, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, or -$NHCONR_{24}R_{25}$, then $NR_{24}R_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from $S(O)_m$, oxygen, nitrogen, and NR_{12}, and optionally containing from one to three double bonds;

R_{26} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocycloalkyl groups of the compound of formula I, II, or III do not comprise any –S-S-, -S-O-, -N-S-, or –O-O- bonds, and do not comprise more than two oxygen or $S(O)_m$ heterologous members.

2. A compound according to claim 1, wherein R_4 is -$NHCH_2CF_3$, -$CONHNH_2$, -$CONHNHCH_3$, –OCF_3, fluoro, -$OCHF_2$, -$OCH_2(C_3$-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkyl), -$SCH_2(C_3$-C_5 cycloalkyl), -S(C_3-C_8 cycloalkyl), –OCH_3, -CH_3, –CH_2CH_3, chloro, bromo, –CF_3, –CH_2OH, –CH_2OCH_3, -CH_2OCF_3, -SCH_3, –$S(O)CH_3$, –$S(O)_2CH_3$, –$C(O)CH_3$, –$NR_{24}R_{25}$, –NO_2, -$CH(OH)CH_3$, or –CN.

3. A compound according to claim 1, wherein R_4 is –$C(O)NR_{24}R_{25}$ or -$C(O)NHNR_{24}R_{25}$.

4. A compound according to claim 1, wherein R_4 is -(C_1-C_4 alkylene)$NR_{24}R_{25}$.

5. A compound according to claim 1, wherein R_4 is –$COOCH_3$ or –$COOCH_2CH_3$.

6. A compound of formula I according to claim 1, wherein Z is O; B is –$NHCHR_1R_2$, wherein R_1 is -C(O)H, -C(O)(C_1-C_6 alkyl), or –C_1-C_6 alkyl, wherein said C_1-C_6 alkyl is optionally substituted with from one to six fluoro atoms or one or two R_8 independently selected from –C_1-C_4 alkyl, hydroxy and –O-(C_1-C_6 alkyl), and wherein R_2 is –C_1-C_{12} alkyl optionally containing from one to three double or triple bonds and optionally substituted with from one three substituents selected from fluoro and C_1-C_8 alkyl; R_5 is phenyl, pyridyl or pyrimidyl, substituted with two or three R_{27} groups selected from halo, -(C_1-C_4 haloalkyl), -$C(O)R_{24}$, -OR_{25}, -$C(O)NR_{24}R_{25}$, and C_1-C_{10} alkyl which is optionally substituted with one to three substituents, preferably one substituent, selected from hydroxy, C_1-C_6 alkoxy, and –$NR_{24}R_{25}$; and R_4 is -$C(O)NR_{24}R_{25}$.

7. A compound of formula I according to claim 1, wherein Z is O; B is -$NHCHR_1R_2$, wherein R_1 of –$NHCHR_1R_2$ is -C(O)H, -C(O)(C_1-C_6 alkyl), or –C_1-C_6 alkyl, wherein said C_1-C_6 alkyl is optionally substituted with from one to six fluoro atoms or one or two R_8 independently selected from –C_1-C_4 alkyl, hydroxy and –O-(C_1-C_6 alkyl), and wherein R_2 of –$NHCHR_1R_2$ is –C_1-C_{12} alkyl optionally containing from one to three double or triple bonds and optionally substituted with from one three substituents selected from fluoro and C_1-C_8 alkyl; R_5 is phenyl, pyridyl or pyrimidyl, substituted with two or three R_{27} groups selected from halo, -(C_1-C_4 haloalkyl), -$C(O)R_{24}$, -OR_{25}, -$C(O)NR_{24}R_{25}$, and C_1-C_{10} alkyl which is optionally substituted with one to three substituents, preferably one substituent, selected from hydroxy, C_1-C_6 alkoxy, and –$NR_{24}R_{25}$; and R_4 is –NR_1R_2, wherein R_1 of –NR_1R_2 is C_1-C_6 alkyl,

C_3-C_8 cycloalkyl, or -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), and R_2 of $-NR_1R_2$ is C_1-C_{12} alkyl optionally containing from one to three double or triple bonds and optionally substituted with from one three fluoro atoms.

8. A compound according to claim 1 selected from:

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-hydroxymethyl-propylamino)-6,N-dimethyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-methoxymethyl-propylamino)-6,N-dimethyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-methoxymethyl-propylamino)-6-methyl-nicotinamide;

2-(4-bromo-2-methoxy-phenoxy)-4-(1-ethyl-propylamino)-6-methyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-ethyl-2-methoxy-propylamino)-6-methyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-ethyl-2-methoxy-propylamino)-6,N-dimethyl-nicotinamide;

2-(4-chloro-2-trifluoromethoxy-phenoxy)-4-(1-ethyl–propylamino)-6-methyl-nicotinamide;

2-(4-chloro-2-trifluoromethoxy-phenoxy)-4-(1-ethyl-propylamino)-6-N-dimethyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1S,2R-1-ethyl-2-methoxy-propylamino)-6,N-dimethyl-nicotinamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1S,2S-1-ethyl-2-methoxy-propylamino)-6,N-dimethyl-nicotinamide;

2-(4-bromo-2-methoxy-phenoxy)-4-(1-ethyl-propylamino)-6-methyl-nicotinonitrile;

4-[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yloxy]-3,5-dimethyl-benzamide;

2-(4-chloro-2,6-dimethyl-phenoxy)-6-methyl-4-(1-methylsulfanylmethyl-propylamino)-nicotinic acid methyl ester;

2-(4-chloro-2,6-dimethyl-phenoxy)-4-(1-hydroxymethyl-propylamino)-6-methyl-nicotinic acid methyl ester;

2-(4-bromo-2,6-dimethyl-phenoxy)-4-(1-ethyl-propylamino)-6-methyl-nicotinonitrile;

2-(4-chloro-2-trifluoromethoxy-phenoxy)-4-(1-ethyl-propylamino)-6-methyl-nicotinic acid methyl ester; and

2-(4-chloro-2,6-dimethyl-phenoxy)-6-methyl-4-(tetrahydro-furan-3-ylamino)-nicotinic acid methyl ester;

and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

10. A method for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as

depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder or condition.

11. A method of treating a condition comprising administering a compound of claim 1 in an amount effective to treat said condition, wherein said condition is selected from the group consisting of:

a) abnormal circadian rhythm;

b) depression, further wherein a second compound for treating depression is administered, said second compound for treating depression having an onset of action that is delayed with respect to that of said CRF antagonist; and

c) emesis.

12. The method of claim 11 wherein the condition is abnormal circadian rhythm, and the compound is combined with a second compound useful for treating a sleep disorder.

13. The method of claim 12, wherein said second compound is selected from the group consisting of tachykinin antagonists, agonists for GABA brain receptors, metalonergic

compounds, GABA brain receptor agonists, $5HT_2$ receptor antagonists, and D4 receptor binding .

14. The method of claim 11 wherein said condition is depression, and wherein said second compound having delayed action for treating depression is selected from the group consisting of selective serotonin reuptake inhibitors, tricyclic antidepressants, norepinephrine uptake inhibitors, lithium, bupropion, sertraline, fluoxetine, trazodone, and a tricyclic antidepressant selected from the group consisting of imipramine, amitriptyline, trimipramine, doxepin, desipramine, nortriptyline, protriptyline, amoxapine, clomipramine. maprotiline, and carbamazepine, and pharmaceutically acceptable salts and esters of the above-recited compounds.

15. The method claim 11 wherein said condition is emesis, further comprising administering a second compound for treating emesis.

16. The method of claim 15 wherein said second compound for treating emesis is selected from the group consisting of tachykinin antagonists, 5HT3 antagonists, GABA agonists, and substance P inhibitors.

17. A pharmaceutical composition for treating a condition comprising a compound of claim 1 in an amount effective to treat said condition and a pharmaceutically acceptable carrier, wherein said condition is selected from the group consisting of:

a) abnormal circadian rhythm;

b) depression, further wherein a second compound for treating depression is administered, said second compound for treating depression having an onset of action that is delayed with respect to that of said CRF antagonist; and

c) emesis.

18. A pharmaceutical composition according to claim 17, wherein the condition is abnormal circadian rhythm, and the compound is combined with a second compound useful for treating a sleep disorder.

19. A pharmaceutical composition according to claim 18, wherein said second compound is selected from the group consisting of tachykinin antagonists, agonists for GABA brain receptors, metalonergic compounds, GABA brain receptor agonists, $5HT_2$ receptor antagonists, and D4 receptor binding .

20. A pharmaceutical composition according to claim 17 wherein said condition is depression, and wherein said second compound having delayed action for treating depression is selected from the group consisting of selective serotonin reuptake inhibitors, tricyclic antidepressants, norepinephrine uptake inhibitors, lithium, bupropion, sertraline, fluoxetine, trazodone, and a tricyclic antidepressant selected from the group consisting of

imipramine, amitriptyline, trimipramine, doxepin, desipramine, nortriptyline, protriptyline, amoxapine, clomipramine, maprotiline, and carbamazepine, and pharmaceutically acceptable salts and esters of the above-recited compounds.

21. A pharmaceutical composition according to claim 17 wherein said condition is emesis, further comprising administering a second compound for treating emesis.

22. A pharmaceutical composition according to claim 21 wherein said second compound for treating emesis is selected from the group consisting of tachykinin antagonists, 5HT3 antagonists, GABA agonists, and substance P inhibitors.